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(19)(CA) **APPLICATION FOR CANADIAN PATENT** (12)

(54) Methods for Inhibiting Uterine Fibrosis

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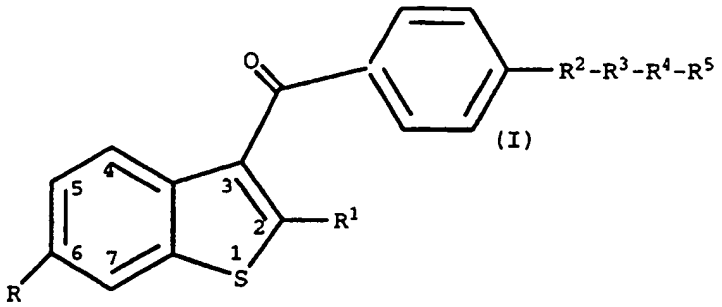
(57) 9 Claims

X-9440

ABSTRACT

A method of inhibiting uterine fibrosis comprising administering to a human in need of treatment an effective amount of a compound having the formula



wherein R is hydrogen; hydroxy; C_1-C_6 alkoxy; a group of the formula -O-C(O)-R^a, wherein R^a is hydrogen, C_1-C_6 alkyl optionally substituted with amino, halo, carbonyl, C_1-C_6 alkoxycarbonyl, C_1-C_7 alkanoyloxy, carbamoyl and/or aryl; or R^a is C_1-C_6 alkenyl optionally substituted with aryl; or R^a is a C_3-C_7 cycloalkyl; or R^a is aryl optionally substituted with hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, and/or halo; or R^a is -O-aryl, said aryl optionally substituted with hydroxy C_1-C_6 alkyl, C_1-C_6 alkoxy, and/or halo,

or R is a group of the formula -O-SO_2-R^b wherein R^b may be C_1-C_6 alkyl or aryl optionally substituted with C_1-C_6 alkyl;

or R is carbamoyloxy wherein the nitrogen may be substituted once or twice with C_1-C_6 alkyl;

or R is a group of the formula -O-C(O)R^c-O-(C_1-C_6 alkyl) wherein R^c is a bond or C_1-C_6 alkanediyl;

R^1 is halo, C_1-C_6 alkyl, C_1-C_7 alkyl substituted with C_1-C_6 alkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, or substituted or unsubstituted C_3-C_7 cycloalkenyl;

R^2 is O or CH_2;

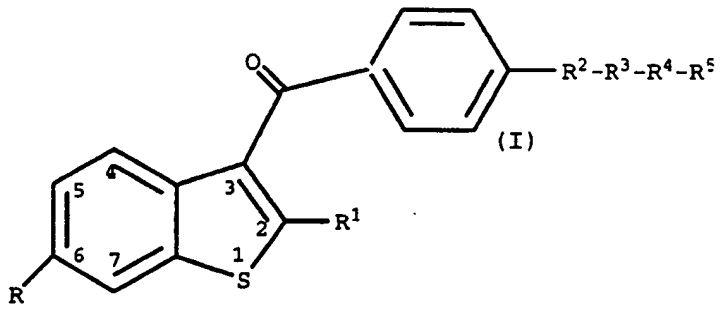
R^3 is CH_2 or $(CH_2)_2$;

R^4 is $-\overset{O}{\overset{\|}{C}}-$, CH_2, or a bond; and

R^5 is amino, nitrilo optionally substituted once or twice with C_1-C_6 alkyl; or an N-heterocyclic ring which optionally has another hetero atom selected from N, O, or S in said ring; or a pharmaceutically acceptable salt or solvate thereof.

We claim:

1. A compound having the formula



wherein R is hydrogen; hydroxy; C_1-C_6 alkoxy; a group of the formula -O-C(O)-R^a, wherein R^a is hydrogen, C_1-C_6 alkyl optionally substituted with amino, halo, carbonyl, C_1-C_6 alkoxycarbonyl, C_1-C_7 alkanoyloxy, carbamoyl and/or aryl; or R^a is C_1-C_6 alkenyl optionally substituted with aryl; or R^a is a C_3-C_7 cycloalkyl; or R^a is aryl optionally substituted with hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, and/or halo; or R^a is -O-aryl, said aryl optionally substituted with hydroxy C_1-C_6 alkyl, C_1-C_6 alkoxy, and/or halo,

or R is a group of the formula -O-SO_2-R^b wherein R^b may be C_1-C_6 alkyl or aryl optionally substituted with C_1-C_6 alkyl;

or R is carbamoyloxy wherein the nitrogen may be substituted once or twice with C_1-C_6 alkyl;

or R is a group of the formula -O-C(O)R^c-O-(C_1-C_6 alkyl) wherein R^c is a bond or C_1-C_6 alkanediyl;

R^1 is halo, C_1-C_6 alkyl, C_1-C_7 alkyl substituted with C_1-C_6 alkyl, substituted or unsubstituted C_3-C_7 cycloalkyl, or substituted or

unsubstituted C_3-C_7 cycloalkenyl;

R^2 is O or CH_2;

R^3 is CH_2 or $(CH_2)_2$;

R^4 is $-\overset{O}{\overset{\|}{C}}-$, CH_2, or a bond; and

R^5 is amino, nitrilo optionally substituted once or twice with C_1-C_6 alkyl; or an N-heterocyclic ring which optionally has another hetero atom selected from N, O, or S in said ring; or a pharmaceutically acceptable salt or solvate thereof, for use in inhibiting uterine fibrosis.

2. A compound according to Claim 1 wherein R^1 is a group having the formula

$$-\underset{\displaystyle (C_1\text{-}C_6\ \text{alkyl})}{\overset{\displaystyle (C_1\text{-}C_6\ \text{alkyl})}{\overset{|}{C}}}-$$

or a cycloalkyl group with a carbon number of three to eight that may be substituted with C_1-C_6 alkyl or hydroxy.

3. A compound of Claim 2 wherein R is hydroxy.

4. A compound according to Claim 3 wherein R^2 is O and R^4 is CH_2.

5. A compound according to Claim 1 wherein said compound is (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-cycloheptylbenzo[b]thien-3-yl) [4-[2-(1-pyrrolidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-cycloheptylbenzo[b]thien-3-yl)[4-[2-(1-

piperidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-isopropylbenzo[b]thien-3-yl)[4-[2-(1-prrolidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-isopropylbenzo[b]thien-3-yl)[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone.

6. A compound according to Claim 3 wherein R^2 is CH_2.

7. A compound according to Claim 6 wherein said compound is (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[3-(1-pyrrolidinyl)propyl]phenyl]methanone, (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[3-(1-piperidinyl)propyl]phenyl]methanone, or (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-pyrrolidinylcarbonyl)ethyl]phenyl]methanone.

8. A compound according to Claim 2 wherein R is C_1-C_6 alkoxy.

9. A compound according to Claim 8, wherein said compound is (6-methoxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone or (6-acetoxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone.

SUBSTITUTE

REMPLACEMENT

SECTION is not Present

Cette Section est Absente